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EXAMINER

BRANNOCK, MICHAEL T

ART UNIT

PAPER NUMBER

1646

DATE MAILED: 03/12/2002

23

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/370,358

Applicant(s)

Sklar et al.

Examiner

Michael Brannock, Ph.D.

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– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Dec 19, 2001

2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-6 and 8-53 is/are pending in the application

4a) Of the above, claim(s) 14 and 18-47 is/are withdrawn from consideration

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-6, 8-13, 15-17, and 48-53 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirements.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

18) ☒ Interview Summary (PTO-413) Paper No(s). 20

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

19) ☐ Notice of Informal Patent Application (PTO-152)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

20) ☐ Other:

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DETAILED ACTION

Status of Application: Claims and Amendments

1. Claims 1-6, 8-47 and new claims 48-53 are pending.
2. Applicant is notified that the amendments put forth in Paper 21, 11/28/01 and Paper 22, 12/19/01, have been entered in full.
3. Claims 14 and 18-47 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, as maintained in Paper 19, 8/28/01

Withdrawn Objections/Rejections:

4. Applicant is notified that all rejections set forth in Paper 19 have been withdrawn in view of Applicant's amendments to the claims set forth in Paper 21.

Applicant's arguments regarding the previous rejections have been fully considered and deemed to be moot in view of Applicant's amendments to the claims and to the new grounds of rejections necessitated by these amendments.

New Rejections:

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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6. Claims 1-6, 8-13 and 15-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 requires the step of "presenting the receptor in conjunction with a support...wherein the receptor in conjunction with a support is analyzed with a flow cytometer". The word "analyzed" in the context of the claim renders the claim indefinite because there is no qualifying information so as to determine what is encompassed by the term "analyzed". A skilled artisan could not know what additional limitations are placed on the claim by the presence of this term. Therefore, the metes and bounds of the claim cannot be determined.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 48, 49, 51 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No: 5583010.

U.S. Patent No: 5583010 disclose methods for non-cellular display (e.g. purified recombinant receptor, col 19, L65) of a 7TM receptor (Growth hormone releasing hormone

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receptor GHRH-R) comprising incorporating an attachment scheme to the receptor (col 20, L1-3), solubilizing the receptor (e.g. col 10, L24), presenting the receptor with in conjunction with a solid support (col 19 L65-col 20 L12), presenting one ligand to bind to the receptor, wherein said ligand is known to the receptor (e.g. GHRH), and combining receptor and ligand to accomplish binding (col 19 L65-col 20 L12). Also, U.S. Patent No: 558310 state that "these assays can be linked to a reporter such as an antibody, biological chemical..., which will express a radioactive, chemical, calorimetric or luminescent signal" see col 20 L4-7; thus one of ordinary skill in the art would understand from this teaching, and particularly from the term "luminescent signal", that it is meant the receptor ligand pairs can be sorted by fluorescence.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 1, 6, 9-13, 15-17, 50, 52 and 53-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No: 5583010 as applied to claims 48, 49 and 51 above, in view of U.S. Patent No: 5639603.

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Claims 1, 6, 9-13, 15-17, 50, 52 and 53-57 require the limitations of claims 48, 49 and 51, as discussed above, yet claims 1, 6, 9-13, 15-17, 50, 52 and 53-57 also stipulate that the method of sorting be flow cytometry and that the solid support be bead substrates appropriate for flow cytometry. Additionally claims 54-57 require that the tag be an epitope tag, e.g. either an N or C-terminal, or internal epitope. One of ordinary skill in the art appreciates that at col 20, first paragraph, U.S. Patent No: 5639603 refers to such attachment means in the statement "Solid phase assays can involve receptor attached to a solid support either chemically or immunologically..."

Although U.S. Patent No: 5583010 appears to be silent with regard to flow cytometry, flow cytometry is a well known method of sorting fluorescently labeled receptor-ligand pairs. U.S. Patent No: 5639603 teaches the general applicability of flow cytometry to the sorting of isolated solubilized receptors and their bound ligands, wherein the solid supports are beads appropriate for flow cytometry and for library screening (see col 31, L40-54). Further, Patent No: 5639603 teaches that the receptor (e.g. col 31, L58) or the ligand (col 36, L35-38) be labeled with a fluorescently labeled marker.

Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made, and with reasonable expectation of success to use beads as the solid support and to separate the receptor-ligand pairs by flow cytometry as taught by U.S. Patent No: 5639603, when practicing the assay of soluble receptors attached to solid supports as taught by U.S. Patent No: 5583010. The motivation to do so was provided by U.S. Patent No: 5639603

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wherein it is taught that "by adopting cell sized solid supports or beads, one can use flow cytometry for high sensitivity receptor binding analysis and facile bead manipulation" (see col 31, L47-54).

11. Claims 2, 3, 4 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No: 5583010, in view of U.S. Patent No: 5639603 as applied to claims 1, 6, 9-13, 15-17, 50, 52 and 53-57 above, and in further view of Robeva, AS *et al.*, *Drug Development Research* 39(243-252)1996.

Claims 2, 3, 4 and 8 stipulate that the tether or attachment means be a C-histidine or an N-histidine tag and that the bead be a Ni-silica bead. The use of histidine tags in the receptor art is old. Further, is well known that Ni-silica beads are used with histidine tags. Robeva *et al.* disclose a method of displaying a 7TM receptor (Adenosine receptor) comprising incorporating an attachment scheme (e.g. hexahistidine tag) into the Adenosine receptor (GPCR construct), solubilizing the receptor by lysing membranes comprising the receptor (page 245), presenting the receptor on a solid support (e.g. Ni-NTA agarose, page 245), wherein said method further comprises the step of combining the receptor and a ligand to accomplish binding (see page 244, col 2). Additionally, whether to use the tag at the N or C-terminal is an obvious matter of routine optimization of operating parameters. Further, Rebeva teach that the step of incorporating an attachment scheme comprises incorporating the tag (coding sequence) into an oligonucleotide: see page 244, MATERIALS AND METHODS, wherein the method of subcloning the Adenosine

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receptor is referenced in Robeva et al., 1996, Biochem. Pharm. 51:545-555, wherein it is indicated that the tags are incorporated using a 30 base pair oligonucleotide, see Robeva et al., 1996, Biochem. Pharm, page 554.

Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made to, with reasonable expectation of success to use histidine tags as taught by Robeva, as the attachment means for the assay disclosed by U.S. Patent No: 5583010 and modified according to the teachings of U.S. Patent No: 5639603, as discussed above. The motivation to do so was provided by Robeva, AS et al., Drug Development Research wherein it is stated that their method should be useful for other proteins and for a variety of methods including reconstitution assays (see page 554), reconstitution assays being required for solubilization of the receptor, as per the instant invention.

Conclusion

No claims are allowable.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period

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will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (703) 306-5876. The examiner can normally be reached on Mondays through Thursdays from 8:00 a.m. to 5:30 p.m. The examiner can also normally be reached on alternate Fridays.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB


March 9, 2002


YVONNE EYLER, PH.D.
SUPERVISORY PATENT EXAMINER
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